

# Psychosocial and Executive Functioning Outcomes in Pediatric Brain Tumor Survivors After Proton Radiation

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October 28, 2022

## Abstract

**Background:** Pediatric brain tumor survivors can experience detrimental effects from radiation treatment. This cross-sectional study examined psychosocial and executive functioning in pediatric patients treated with proton radiation (PRT). **Procedure:** Parents of 187 brain tumor survivors completed standardized scales [?]1 year after PRT. One-way analysis of variance, Pearson correlation, and chi-square analysis were used to determine the impact of demographic, diagnostic or treatment-related characteristics. One-sample t-tests compared mean scores with published normative means. Rates of impairment (T-score >65) were calculated. **Results:** Mean age at PRT (baseline) was 8.49 years; mean follow-up interval 3.84 years. Approximately one-third (36.9%) received craniospinal irradiation (CSI). All mean T-scores for psychosocial and executive functioning were within the normal range. Younger age at baseline correlated with more behavior problems; older age with more problems with adaptive skills. Baseline age was not correlated with executive functioning. Follow-up interval and radiation field (CSI; focal) were not related to psychosocial or executive problems. Significantly elevated mean T-scores were in withdrawal ( $p < 0.001$ ) and metacognitive skills (e.g., working memory  $p < 0.001$ ); significantly lower ( $p < 0.05$ ) in hyperactivity, aggression, conduct problems, adaptability, social skills, and behavioral regulation. Rates of impairment far exceeded expectation in overall metacognitive skills (18.7%), withdrawal (17.9%), and activities of daily living (15.0%). Impairment rates were not related to age at PRT or radiation field. **Conclusions:** Psychosocial and executive functioning was within the normal range, on average, at follow-up. However, elevated impairment rates were observed in specific aspects of functioning (e.g., withdrawal, metacognitive executive functioning). Targeted screening and proactive intervention are needed.

## Introduction

Brain tumors are the most common type of solid tumor in children.<sup>1</sup> Radiation treatment is a life-saving intervention that can be associated with neurocognitive, emotional, and behavioral sequelae,<sup>2-7</sup> although the use of proton radiation treatment (PRT) has yielded more favorable outcomes due to its dose-sparing properties.<sup>8-10</sup> Many studies examining the outcomes of PRT revealed cognitive and adaptive functioning in the normal range more than 3 years post-treatment;<sup>11-13</sup> however, adaptive functioning challenges at 5 years post-PRT have been observed, with greater vulnerability in survivors treated with craniospinal irradiation (CSI).<sup>12</sup> Studies of psychosocial and executive functioning outcome following PRT in pediatric brain tumor survivors are relatively recent, and require replication to strategically guide intervention. Challenges with social functioning have been described,<sup>14</sup> most notably in aspects of peer exclusion and isolation. While post-PRT studies examining executive functioning have revealed normal functioning as a group,<sup>15-16</sup> relative weaknesses in processing efficiency<sup>15-16</sup> were observed and may contribute to functional limitations among some patients.

Studies have revealed higher rates of internalizing emotional problems characterized by depression and anxiety following conventional radiation<sup>17-19</sup> whereas externalizing behavior problems (aggression, defiance) are not elevated,<sup>20-21</sup> with rates lower than the normative mean.<sup>22</sup> Greater inattention (internally experienced

symptom) has been reported on parent questionnaires, whereas greater hyperactivity (externally observed behavior) has not.<sup>23-24</sup> As a whole, pediatric survivors treated with radiation tend to experience higher rates of symptoms that are experienced inside one's mind (internalizing) rather than symptoms that are more readily observed and directed towards other people (externalizing).

Social functioning is also impacted at higher rates following radiation treatment with higher rates of social isolation,<sup>6,23,25</sup> reduced social acceptance<sup>2,26</sup> and withdrawal.<sup>17</sup> Pediatric brain tumor survivors were significantly less likely to be able to name a friend compared with youth who underwent treatment for non-central nervous system (CNS) tumors,<sup>27</sup> suggesting that treatment-related factors (e.g., school absence, reduced socialization) cannot fully account for their challenges. Reduced leadership skills among survivors have also been described.<sup>2,23</sup> Studies have collectively demonstrated weaknesses in social responsiveness and engagement levels, rather than deficits in social skills themselves. A recent post-PRT study examining social functioning observed challenges with social relationships characterized by social exclusion and reduced amount of friendships.<sup>14</sup>

Executive functions are a group of higher ordered cognitive skills that represent a constellation of behaviors required for task completion and goal-directed behavior.<sup>24</sup> Executive functions are mediated by frontal-subcortical-cerebellar white matter circuits which are highly susceptible to injury from radiation treatment,<sup>28-29</sup> affecting the developmental trajectory. Executive functioning is affected at higher rates following radiation compared to the general population.<sup>20,22,25,30-32</sup> Ecological assessment using parent-report is a valuable method to capture executive functioning abilities in daily contexts.<sup>33</sup> Parent reports have revealed greater levels of executive dysfunction in pediatric brain tumor survivors following radiation treatment, most notably in metacognitive executive skills: working memory, planning/organization, and initiation.<sup>19, 34-35</sup> Reports of difficulty with behavioral dysregulation are mixed, with some studies citing significantly more difficulty<sup>34,36</sup> and others reporting lower rates of behavioral dysregulation.<sup>37</sup> Fewer problems with inhibition have been reported.<sup>19,35</sup>

Several specific risk factors may lead to adverse outcomes for pediatric brain tumor survivors. Younger age at diagnosis and treatment is a high risk factor for greater neurocognitive,<sup>12,13,22</sup> emotional, and behavioral<sup>22,37</sup> sequelae. The extent of radiation (CSI vs. focal) also impacts cognitive outcomes,<sup>12,13,38</sup> including executive functioning.<sup>15</sup> Socioeconomic status (SES) can adversely impact functional outcomes in pediatric oncological survivors,<sup>39</sup> including pediatric patients diagnosed with brain tumors.<sup>40-41</sup> Examination of risk factors following post-PRT is important to guide psychosocial treatment for pediatric survivors treated with PRT, as current studies reveal inconsistent relationships with specific treatment and demographic variables.<sup>12-16</sup> Identifying predictive variables can help direct interventions to those most vulnerable.

The goal of the current study was to examine whether pediatric brain tumor survivors treated with PRT had problems with psychosocial and executive functioning at follow-up. The study examined demographic, diagnostic, and treatment-related variables to identify those patients at high risk for adverse outcome. For the purposes of this study, psychosocial is broadly defined to include emotional, behavioral, adaptive, and social domains of functioning. Executive functioning was also examined given report of post-radiation impact in the literature.<sup>12,14,16</sup> It was anticipated that: 1) psychosocial and executive functioning for the total sample would be within the normal range; 2) significant problems with behavioral dysregulation and externalizing behaviors would not be seen; 3) a longer time interval between PRT and follow-up would be associated with greater problems, and 4) demographic factors would impact outcomes.

## Methods

### Participants and Procedures

This follow-up cross-sectional study consisted of 187 patients treated with PRT for a primary brain tumor. Patients received assessment during PRT (baseline) as part of their routine clinical care at a scheduled outpatient visit. Eligibility criteria for this analysis included diagnosis of any type of brain tumor, patients were [?] 20 years at initiation of PRT, patients had no prior diagnosis of brain or CNS tumor, no recurrence, and follow-up assessment was conducted at least one year post-PRT. Follow-up assessment consisted of

standardized written measures assessing psychosocial and executive functioning with age-based normative data (Table 1).

Patients were treated with PRT, surgery, and chemotherapy appropriate for the diagnosis and according to the current standard of care. Surgical resection, when performed, was prior to PRT. Chemotherapy was completed before follow-up testing. Radiation was delivered with standard fraction sizes of 1.8 Gy (RBE) per fraction (1.5 Gy per fraction for germinomas) in accordance with the national standard set by Children's Oncology Group protocols for target coverage. Institutional Review Board approvals were obtained for this study.

## Statistical Analyses

Descriptive statistics were used to characterize the sample at baseline and follow-up. The Behavior Assessment System for Children (BASC)<sup>42-43</sup> Behavioral Symptoms Index and Adaptive Skills Composite and the Behavior Rating Inventory of Executive Functioning (BRIEF)<sup>44-45</sup> Global Executive Composite, Behavioral Regulation Index, and Metacognition Index were used as primary outcome measures. One-way analysis of variance (ANOVA) was conducted to determine the differential impact of demographic, diagnostic, and treatment-related characteristics on these primary outcome measures. Pearson correlation was used to investigate the relationship between the primary outcome measures by age at baseline, SES, and the time interval between baseline and follow-up.

One-sample t-tests were used to compare mean T-scores with published normative means. Rates of impairment were calculated and defined as the frequency of scores > 1.5 S.D. above the mean of 50 (T-score > 65). Chi-square test of independence was conducted to evaluate the differences in rates of impairment by radiation field (CSI or focal). One-way ANOVA was performed to evaluate the rates of impairment by age at baseline.

Analyses were performed using SPSS version 24 (IBM 2016, Chicago, IL). Two-tailed analyses were used in all comparisons; statistical significance was defined as  $p < 0.05$ .

## Results

### Participants

As shown in Table 2, the mean age at baseline was 8.49 years (range, 1.05 to 20.41). The mean length of follow-up was 3.84 years (range, 1.00 to 14.39 years). All patients received PRT of which 69 (36.9%) received CSI. There was no significant difference between age at baseline and the CSI and focal radiation groups ( $F(1, 185) = 2.1, p = 0.149$ ). More than half (64.7%) received both PRT and chemotherapy. Most (85.0%) underwent gross or near/subtotal surgical resection prior to PRT. Medulloblastoma was the most common histology group (29.4%). Histology was significantly related to age at baseline ( $F(5, 181) = 11.43, p < 0.001$ ); the ependymoma group was younger (Mean = 5.78 years, S.D. = 4.34) than the other histology groups while the germ cell tumor group (Mean = 13.82 years, S.D. = 2.70) was older. The majority of patients were White (92.5%). The average median household income in the community of residence<sup>44-45</sup> was \$83,664 (range, \$34,118 to \$213,750).

### Psychosocial Functioning

All BASC mean T-scores were in the normal range at follow-up (Table 3), although scores were variable ranging from within the normal range to the impaired range across most scales. There was a significant negative correlation between age at baseline and the Behavioral Symptoms Index ( $r = -0.19, n = 187, p = 0.01$ ) and a positive correlation with age at baseline and the Adaptive Skills Composite ( $r = 0.29, n = 187, p < 0.001$ ). That is, younger patients at baseline had more behavior problems at follow-up while older patients had more problems with adaptive skills. Histology was significantly related to the Behavioral Symptoms Index mean T-scores ( $F(5, 181) = 2.41, p < 0.05$ ); the ependymoma group had a higher score on average ( $M = 51.29, S.D. = 8.78$ ) than the other histology groups, although near the mean for age. No significant relationship was found between the Adaptive Skills Composite mean T-scores and histology ( $F(5, 181) =$

1.22,  $p = 0.30$ ). No significant relationships ( $p$  values  $[?] 0.10$ ) were found between the Behavioral Symptoms Index or the Adaptive Skills Composite mean T-scores and the following factors: gender, hydrocephalus at diagnosis, history of surgical resection, tumor location or treatment with chemotherapy. Neither the Behavioral Symptoms Index nor the Adaptive Skills Composite T-scores were significantly correlated with the time interval between baseline and follow-up ( $p$  values  $[?] 0.33$ ) or with SES ( $p$  values  $[?] 0.39$ ). Notably, radiation field was not significantly related to the mean T-scores for the Behavioral Symptoms Index ( $F(1, 185) = 0.59$ ,  $p = 0.45$ ) or the Adaptive Skills Composite ( $F(1, 185) = 0.28$ ,  $p = 0.60$ ). No further analyses were conducted of the interaction between radiation field and age at baseline since mean T-scores for these two measures were not significantly different by radiation field and age at baseline was not significantly related to radiation field.

Compared to the normative mean, a statistically significantly elevated mean T-score was found in Withdrawal ( $t(172) = 3.89$ ,  $p < 0.001$ ) while mean T-scores were significantly lower (indicating less problems) than expectation in Hyperactivity ( $t(172) = -3.54$ ,  $p < 0.01$ ), Aggression ( $t(169) = -7.72$ ,  $p < 0.001$ ), Conduct Problems ( $t(149) = -7.93$ ,  $p < 0.001$ ), Adaptability ( $t(170) = -2.52$ ,  $p < 0.05$ ), Social Skills ( $t(171) = -4.78$ ,  $p < 0.001$ ), and the Behavioral Symptoms Index ( $t(186) = -2.17$ ,  $p < 0.05$ ). Mean T-scores were at or near the normative mean on the remaining BASC scales ( $p$  values  $[?] 0.06$ ), including Anxiety, Depression, Somatization, Attention Problems, and the Adaptive Skills Composite.

Rates of impairment for the Behavioral Symptoms Index and Adaptive Skills Composite were similar to expected rates in the general population as were the rates of impairment on the following clinical and adaptive scales: Hyperactivity, Aggression, Conduct Problems, Depression, Anxiety, Atypicality, Attention Problems, Adaptability, Social Skills, Leadership, and Functional Communication. In contrast, rates of impairment in Withdrawal (17.9%), Activities of Daily Living (15.0%), and Somatization (12.5%) scales exceeded expectations. There were no significant differences between rates of impairment and radiation field on any scale ( $p$  values  $[?] 0.10$ ) or between rates of impairment and age at baseline on any scale ( $p$  values  $[?] 0.15$ ).

## Executive Functioning

All BRIEF mean T-scores were in the normal range (Table 2), although scores ranged from within the normal range to the impaired range across most scales. There were no significant correlations between the Global Executive Composite, Behavioral Regulation Index or Metacognition Index T-scores and age at baseline ( $p$  values  $[?] 0.34$ ), time interval between baseline follow-up ( $p$  values  $[?] 0.29$ ) or SES ( $p$  values  $[?] 0.54$ ). The mean T-scores for these three primary outcome measures were also not significantly related ( $p$  values  $[?] 0.10$ ) to the following variables: gender, histology, hydrocephalus at diagnosis, history of surgical resection, location of tumor or treatment with chemotherapy. Radiation field was not significantly related to the mean T-scores for the Global Executive Composite ( $F(1, 185) = 0.14$ ,  $p = 0.71$ ), Behavioral Regulation Index ( $F(1, 185) = 0.07$ ,  $p = 0.80$ ) or Metacognition Index ( $F(1, 185) = 0.22$ ,  $p = 0.64$ ). No further analyses were conducted of the interaction between radiation field and age at baseline since mean T-scores for these three measures were not significantly different by radiation field and age at baseline was not significantly related to radiation field.

Compared to the normative mean, statistically significantly elevated mean T-scores were found on the Metacognition Index ( $t(186) = 3.01$ ,  $p < 0.01$ ) and the Initiate ( $t(163) = 3.34$ ,  $p < 0.01$ ), Working Memory ( $t(186) = 5.51$ ,  $p < 0.001$ ), and Plan/Organize ( $t(185) = 2.73$ ,  $p < 0.01$ ) scales. In contrast, mean T-scores were significantly better than expectation on the Inhibit scale ( $t(186) = -3.28$ ,  $p < 0.01$ ) and the Behavioral Regulation Index ( $t(186) = -2.36$ ,  $p < 0.05$ ). Mean T-scores were at or near the normative mean on the Global Executive Composite and the remaining clinical scales.

Rate of impairment on the Behavioral Regulation Index was similar to expected rates in the general population as were the rates of impairment on the Inhibit, Shift, Emotional Control, and Self-Monitor scales. In contrast, rates of impairment in Working Memory (25.1%), the Metacognition Index (18.7%), Initiate (18.3%), Plan/Organize (17.2%), and the Global Executive Composite (15.0%) far exceeded expectations.

There were no significant differences between rates of impairment and radiation field on any scale ( $p$  values [?] 0.09) or between rates of impairment and age at baseline on any scale ( $p$  values [?] 0.22).

## Discussion

The present study examines psychosocial and executive functioning outcomes in a large cohort of pediatric brain tumor survivors at an average of 3.84 years post-PRT. Mean scores were not significantly different from normative expectation for psychosocial and executive functioning at follow-up. However, rates of impairment in social withdrawal, activities of daily living, and metacognitive executive functioning skills were markedly higher than would be expected in the general population. These results are largely consistent with the growing body of literature among pediatric brain tumor survivors post-PRT that report sample means in the normal range for many aspects of emotional and behavioral functioning whereas problems are often reported at a higher level with social and executive functioning.<sup>14</sup>

Favorably, the current findings revealed significantly less behavior problems (hyperactivity, aggression) compared to normative expectations consistent with previous studies.<sup>20-22</sup> Problems with depression or anxiety were not identified, an important finding with regard to quality of life. However, a relatively large proportion of patients (12.5%) was rated as having problems with somatization and were viewed by their parents as having more physical complaints/discomforts;<sup>42-43</sup> not surprising given the complex medical history of brain tumor survivors.

A large proportion of survivors were rated as having impairment in social withdrawal ([?]18%) (a tendency to evade others to avoid social contact)<sup>42-43</sup> although their social skills were within the normal range with a low rate of impairment, suggesting survivors have the skills necessary for interacting successfully with peers and adults. This finding is consistent with prior literature on conventional post-radiation outcomes reflecting greater social withdrawal,<sup>17</sup> isolation,<sup>2,6,23,25</sup> and lower acceptance,<sup>2,26</sup> but lacking deficits in social cognition skills (knowledge about how to appropriately interact). Reduced prosocial skills (complimenting others, offering help) were observed in a post-PRT study<sup>14</sup> reflecting the need for further exploration of this specific aspect of socialization.

The higher rate of challenges with activities of daily living (15%) is consistent with prior research that identified greater adaptive skills impairment among a more homogenous sample of youth 5 years post-PRT, particularly in the domains of practical and social skills.<sup>12</sup> While the mean for our total sample did not exceed normative expectation, the rate of impairment in activities of daily living and the recent finding in the literature warrant continued attention to the development of these skills. Metacognitive executive functioning was the area of greatest concern reported by parents in this study, consistent with the literature.<sup>19,34-35</sup> Significantly more survivors were rated as having problems with aspects of metacognitive executive functioning skills (up to 25%), which includes the ability to take initiative, sustain working memory (e.g., capacity to hold and “work on” information in mind to complete an activity), and plan and organize tasks.

Previous research has indicated an association between problems with psychosocial and executive functioning and time interval following PRT.<sup>14,46</sup> However, this finding was surprisingly not revealed in this sample. In fact, most demographic and treatment-related factors examined did not significantly impact psychosocial and executive functioning outcomes in this sample, including gender, race, SES, tumor location, radiation field, history of surgery, or chemotherapy. While some studies have identified relationships between PRT treatment variables (hydrocephalus, time since treatment) and social outcomes,<sup>14</sup> these patterns are not universal.

Age at baseline and histology were the only factors that had significant relationships with outcomes; younger ages at baseline and those diagnosed with ependymoma (youngest histology group at baseline) had more behavior problems and older ages at baseline had more problems with adaptive skills at follow-up. Prior research has noted greater emotional and behavioral difficulty associated with younger age at treatment.<sup>22,37</sup> For older ages, the inability to meet increasing expectations to carry out tasks with greater independence with advancing age may reflect the high rate of metacognitive executive challenges found in this sample.

Psychosocial and executive functioning outcomes should be understood in the context of various environmental and situational factors (extended absences from school, reduced opportunities for peer interactions, development of everyday living skills). The impact of tumor-related symptoms prior to diagnosis (e.g., tailored treatment interventions, premorbid developmental and genetic patterns) also need to be considered. Similarly, the major role of parents and health care professionals during their treatment course may contribute to deviations in typical developmental trajectories that may not be accounted for by late effects alone. Taken together, these factors may contribute to, but do not fully account for,<sup>27</sup> the disruption of normal development of psychosocial and executive functioning.

These findings highlight both the importance of routine targeted screening (rating scales/questionnaires) for emerging challenges in psychosocial and executive functioning in pediatric brain tumor survivors treated with PRT, as well as the need for targeted proactive interventions. Such interventions could target the development of social initiative and participation, independence in adaptive skills, and metacognitive executive functioning skills. For example, interventions that provide increased opportunities for positive social interactions with peers in the context of adult-facilitated support appropriate for age may minimize social withdrawal and maximize social initiation and engagement. Patients may benefit from explicit instruction or coaching in executive functioning that teaches them age-appropriate strategies to plan, organize, set goals, prioritize, multi-task, and be a self-starter and independently problem solve. Cognitive remediation,<sup>47-49</sup> cognitive-behavioral therapy,<sup>46</sup> social skill programming,<sup>50-51</sup> and psychopharmacology<sup>52-53</sup> each have been shown to be effective for pediatric brain tumor survivors. Methylphenidate may be beneficial for some patients following PRT as long-term improvements in both social functioning and withdrawal have been reported.<sup>52</sup>

A strength of the current study is the large cohort of pediatric brain tumor survivors in the sample. While these results contribute to the growing knowledge of psychosocial and executive functioning outcomes of pediatric brain tumor survivors treated with PRT, several limitations of the present study should be noted. First, the cross-sectional study design precludes direct analysis of change over time. Longitudinal studies are needed to examine change in order to identify the emergence and trajectory of psychosocial and executive functioning challenges and to guide targeted screening and proactive intervention efforts. Second, the mean follow-up time interval in this study is relatively short. Late effects of radiation therapy have been well established<sup>29</sup> and psychosocial and executive functioning challenges may emerge later than the mean time interval observed. However, the time interval since PRT and follow-up was not correlated with the primary outcome measures in the present study. Third, the sample was predominantly White and of relatively high SES, with an estimated median income higher than that of the United States. This homogenous profile may not be representative of patients who receive similar treatment at other medical centers and the results need to be viewed in this context. In addition, patients who received follow-up assessment may have parents with greater concerns regarding their child's outcome, possibly resulting in a sample that is not representative of all pediatric brain tumor survivors. Finally, the current findings are based only on parent rating scales, which are subject to rater bias and can reflect parents' impressions.

In summary, although psychosocial and executive functioning were, on average, in the normal range in this large cohort of pediatric brain tumor survivors, significant problems were found with social withdrawal, activities of daily living, and metacognitive executive functioning skills. However, no significant problems were evident with depression, anxiety, inattention, hyperactivity, conduct, behavioral dysregulation or overall adaptive skills. Age at baseline was related to problem behaviors and adaptive skills: Younger patients tended to have problem behaviors at follow-up whereas older patients struggled with independent adaptive or everyday living skills. Neither time interval since PRT nor radiation field were related to outcome. Future research will examine a longer follow-up interval to better determine the risk of late effects of PRT.

**Conflict of Interest:** No actual or potential conflicts of interest exist for any author. Torunn Yock receives in kind research support from MIM software.

**Acknowledgments:** The authors thank the MGH Francis Burr Proton Center pediatric patients and their families for participation in this study. This project was supported in part by the Federal Share of program income earned by the Massachusetts General Hospital on C06 CA059267 Proton Therapy Research and

Treatment Center to Margaret Pulsifer and is registered at NCT01180881 ClinicalTrials.gov.

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TABLE 1 Psychosocial and executive functioning outcome measures

Domain	Measure	Forms	Description	Variables
Psychosocial Functioning	Behavior Assessment System for Children (BASC)	Preschool (ages 2-5) Child (ages 6-11) Adolescent (ages 12-21)	Assesses social, emotional, adaptive and behavioral functioning	Behavioral Symptoms Index Adaptive Skills Composite
	Behavior Rating Inventory of Executive Functioning (BRIEF)	Preschool (ages 2-5) Child and adolescent (ages 5-18) Adult (ages 18+).	Assesses executive functioning/ self-regulation in everyday life	Behavioral Regulation Index Metacognition Index Global Executive Composite

The BASC<sup>42-43</sup> and BRIEF<sup>44-45</sup> are standardized written measures with age-based norms. Not all clinical and adaptive scales are produced for the three forms of the BASC. All scores are T-scores (Mean = 50; standard deviation [S.D.] = 10), where higher scores indicate greater problems. All results are presented in the same direction; the results for select scales were transformed for these analyses to be consistent across measures.

TABLE 2 Patient characteristics of the total sample (N = 187)

	Mean ( $\pm$ SD) or n (%)
Mean Age at Baseline (year)	8.49 ( $\pm$ 4.57), range 1.05–20.41
Mean Age at Follow-up (year)	12.33 ( $\pm$ 4.89), range 2.60 – 21.61
Mean Follow-Up Interval (year)	3.84 ( $\pm$ 2.68), range 1.00 – 14.39
Male / Female	99 (52.9) / 88 (47.1)
Race	
White	173 (92.5)
Black or African-American	7 (3.7)
Other	7 (3.7)
Median household income in community of residence*	\$83,664, range \$34,118–\$213,750
Histology	
Medulloblastoma	55 (29.4)
Ependymoma	42 (22.5)
Craniopharyngioma	29 (15.5)
Glial (astrocytoma; glioma)	27 (14.4)
Germ cell	16 (8.6)
Other	18 (9.6)
Primary Tumor Location	
Infratentorial	95 (50.8)
Supratentorial	92 (49.2)
Hydrocephalus at diagnosis	
Yes	83 (44.4)
No	104 (55.6)
Radiation Field	
Craniospinal	69 (36.9)
Focal	118 (63.1)
Surgery (before proton radiation)+ Gross total resection	105 (56.1)

	Mean ( $\pm$ SD) or n (%)
Near/subtotal resection	54 (28.9)
Biopsy	16 (8.6)
None	12 (6.4)
Chemotherapy treatment (yes)	121 (64.7)

\* Median household income in community of residence, a proxy indicator of SES, was derived from patients' residential zip codes at follow-up using U.S. census data.<sup>54-55</sup>

+ No surgical biopsies or resections were performed during or after proton radiation.

TABLE 3 Psychosocial and executive functioning outcome data (N = 187).

Measure	Mean T-score (S.D.)	Range	% Rate of Impairment+
BASC-Parent Report			
Behavioral Symptoms Index (N = 187)	48.57 (9.01)*	32 - 72	3.7
Hyperactivity (N = 173)	47.30 (10.04)**	33 - 89	6.9
Aggression (N = 170)	45.87 (6.97)**	37 - 84	1.8
Conduct problems (N = 150)	44.86 (7.94)**	34 - 83	2.7
Depression (N = 172)	50.28 (10.32)	33 - 91	5.2
Anxiety (N = 173)	50.64 (9.78)	29 - 84	9.2
Somatization (N = 176)	51.65 (11.76)	33 - 105	12.5
Atypicality (N = 172)	48.95 (9.94)	38 - 113	8.1
Withdrawal (N = 173)	53.69 (12.48)**	34 - 92	17.9
Attention problems (N = 172)	48.48 (10.78)	29 - 76	8.7
Adaptive Skills (N = 187)	48.47 (11.21)	22 - 79	7.0
Adaptability (N = 171)	48.02 (10.30)*	27 - 71	5.3
Social Skills (N = 172)	46.34 (10.06)**	28 - 73	2.3
Activities of Daily Living (N = 173)	50.81 (12.20)	18 - 72	15.0
Leadership (N = 153)	49.70 (11.66)	21 - 79	10.5
Functional Communication (N = 173)	50.24 (11.76)	10 - 73	9.8
BRIEF - Parent Report			
Global Executive Composite (N = 187)	51.21 (11.68)	31 - 82	15.0
Behavioral Regulation Index (N = 187)	48.26 (10.08)*	31 - 78	7.5
Inhibit (N = 187)	47.78 (9.24)**	34 - 78	8.0
Shift (N = 187)	50.37 (11.49)	34 - 91	11.2
Emotional Control (N = 187)	48.65 (10.57)	35 - 78	9.1
Self-Monitor (N = 160)	49.17 (11.26)	28 - 82	11.9
Metacognition Index (N = 187)	52.78 (12.62)**	31 - 88	18.7
Initiate (N = 164)	53.26 (12.31)**	36 - 87	18.3
Working Memory (N = 187)	55.52 (13.70)**	36 - 87	25.1
Plan/ Organize (N = 186)	52.48 (12.42)**	33 - 82	17.2
Organization of Materials (N = 165)	49.75 (10.91)	32 - 72	11.5

Note: BASC = Behavior Assessment System for Children<sup>42-43</sup>; BRIEF = Behavior Rating Inventory of Executive Function<sup>44-45</sup>; S.D. = standard deviation

\*  $p < 0.05$  compared to normative means

\*\*  $p < 0.01$  compared to normative means

+ Impairment defined as  $> 1.5$  S.D. above the published normative mean; approximately 7% is  $> 1.5$  S.D. BASC and BRIEF normative mean = 50, S.D. = 10, where higher scores indicate greater problems.